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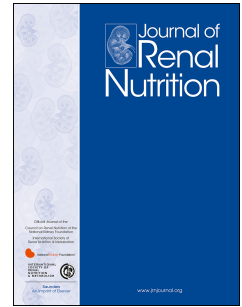
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Functional Nutrition, Naturopathic Nutrition, and Integrative and Holistic Renal Nutrition in Kidney Health and Value-Based Kidney Care Models

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In-This-Issue JREN editorial for September 2022

Title:

**Functional Nutrition, Naturopathic Nutrition, and Integrative and
Holistic Renal Nutrition in Kidney Health and Value-Based Kidney
Care Models**

(Running Head: Functional Nutrition in Kidney Care)

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TEXT starts here

The concept of functional nutrition was originally developed as a holistic nutritional and dietary approach for optimal physiologic functioning of cells as the root cause of health and disease.^{1,2} Functional nutrition is an offspring of the broader discipline, functional medicine, a patient-centered approach to disease management based on the premise that every individual is different from genetics to biochemical and environmental constellations, while considering the holistic picture of physical, mental, emotional, and even spiritual health of the person.^{1,3} To that end, functional nutrition is the main pillar of functional medicine and its integrative multimodal approaches to health and disease.^{4,5} A related analogy is precision nutrition that is aligned with precision medicine.⁶ Functional medicine, through its functional nutrition, aims to correct problems in organ systems using naturopathic and alternative nutritional and dietary approaches that are individualized for a given person at a given stage and form of a disease state, such as chronic kidney disease (CKD). Functional medicine reiterates lifestyle modifications to address health problems, including dietary strategies, physical activity and exercise, sleep management, and other aspects of usual life. Other examples of functional medicine include chiropractic, osteopathic, naturopathic and culinary medicine, acupuncture, body massage and movement therapies, meditation, and dietary regimens.

The field of functional nutrition is based on identifying and recommending functional foods, also known as nutraceuticals, that can provide health benefits beyond basic nutrition and that are used medicinally to manage acute and chronic diseases including their unpleasant symptoms.⁷ Hence, functional nutrition is not only consistent with precision nutrition^{6,8} but also with culinary medicine or “food as medicine”, an important conceptual model under the “World Kidney Recipes”.^{9,10} The Academy of Nutrition and Dietetics has stated that all foods are functional at some physiological levels if they have a potentially beneficial effect on health when

consumed as part of a varied diet, including: 1) conventional whole foods, such as garlic, nuts, and tomatoes that are often recommended to correct inflammation and oxidative stress; 2) modified foods including fortified (such as calcium added or iodized juices and salts), enriched (such as folate enriched breads), and enhanced foods (that are formulated with bioactive components such as with fish oil and ginkgo biloba); 3) medical foods such as phenylketonuria formulas that are free of this amino acid; and 4) foods for special dietary use such gluten-free or lactose-free foods.¹

As for the role of functional nutrition in renal medicine ([Figure 1](#)), it is not quite clear how personalized nutritional and dietary approaches using functional foods can be recommended and implemented for kidney disease management to be scientifically sound, pragmatic, and patient-centered, with acceptable levels of safety, efficacy and adherence. A recently developed example is plant dominant (PLADO) low-protein diets designed for slowing CKD progression and delaying dialysis initiations.¹¹⁻¹³ PLADO diet regimens, managed by trained dietitians in the form of medical nutritional therapy (MNT),^{9, 14-16} can vary in the quantity and quality of protein content and proportion of plant- vs animal-based protein. It has been recommended that more than 2/3 of protein of PLADO regimens should be from plant-proteins to slow CKD progression, as opposed to an often-implemented low potassium “renal diet” that is potassium-centric and hence usually with more than 2/3 of protein from animal-based sources.¹⁶ Given individualized approaches under functional and precision nutrition, low and very low protein diets with dietary protein intake (DPI) of 0.6-0.8 g/kg/day and <0.6 g/kg/day, respectively, are recommended for non-dialysis CKD; moderate protein diets (DPI 0.8-1 g/kg/day) are recommended for those at high risk of CKD such as solitary kidney; and high protein diets (DPI >1.2 g/kg/day) are recommended for dialysis dependent patients and acute kidney injury.¹⁷⁻¹⁹ PLADO, which is

also consistent with pescatarian or lacto-ovo-vegetarian diets, can be a pure vegan diet in its most extreme form,^{13, 20-22} or it can be in the form of Plant Focused Nutrition for CKD in Diabetes (PLAFOND), which includes foods with a low glycemic index.¹⁶ PLADO diet regimens including PLAFOND should be provided under MNT with periodic review of renal dietitians that can be in the form in-person visits or telenutrition.²³ Integrative and functional nutrition is an area of renal nutrition and dietetics practice in which critical thinking skills of renal dietitians are especially important to achieve and maintain the expected level of consistency in providing kidney nutrition care and utilizing evidence-based guidelines and emerging scientific data when available. Given limited evidence-based practice guidelines for functional nutrition in renal care, renal dietitians should use critical thinking skills to appraise the available scientific literature in the context of real-world practice scenarios in kidney care including in the context of emerging value-based kidney care models.²⁴

In this issue of the *Journal*, Wolfe²⁵ reviews scientific evidence behind the link between loneliness as an overlooked contributing factor in anorexia of older adults with End-Stage Renal Disease (ESRD) and highlights loneliness as a focal point for interventions to help improve nutritional status, given the projected rise in the prevalence of ESRD patients who will be living alone. The potential role of functional nutrition in addressing the implications of loneliness for this nutritionally vulnerable population is an important unmet need and warrants more research.

Groesbeck²⁶ studied the perceived value of the board Certified Specialist in Renal Nutrition (CSR) credential among registered dietitian nutritionists (RDN) using an internet-based survey sent to 553 RDNs who held the CSR credential. Based on the response rate of 33% from 184 RDNs, the statements with the highest percent agreement were "validates specialized

knowledge" and "provides evidence of professional commitment", as opposed to "increases salary". Hence, RDNs appear to have a high perceived value of the CSR credentialing, and future research should explore the potential of CSR education to promote functional nutrition focused MNT and practice in support of value-based kidney care models.^{9, 15, 24}

Toussaint et al²⁷ examined the relationship between urinary phosphorus-to-creatinine ratio and survival in the national "Australian Diabetes, Obesity and Lifestyle" cohort of 10,014 participants and found that although no overall association was observed in multivariate analyses, a significant relationship was found between this urinary marker of phosphorus metabolism and mortality in those without CKD. It would be interesting to explore whether kidney health focused functional nutrition by lowering dietary phosphorus load can improve outcomes including kidney and person longevity across populations.

Dahl et al²⁸ studied 217 patients with CKD in a cross-sectional study, including 112 with pre-dialysis CKD stages 3-5, 33 with hemodialysis, and 72 with kidney transplant and found that the number of prescribed medications was inversely associated with mid-upper arm circumference, skinfold thickness triceps, handgrip strength, serum albumin, and hemoglobin. Of note, prescription of medications with nausea as a side-effect showed similar associations, whereas prescription of medications with xerostomia as a side-effect was associated with lower handgrip strength. The impact of polypharmacy on nutritional status of persons with CKD and the potential role of functional nutrition warrant additional studies.

Soohoo et al²⁹ examined the obesity paradox in the form of associations of body mass index (BMI) with all-cause and cause-specific mortality across CKD stages in 2,703,512 patients with BMI data between 2004 and 2006 and performed bias analysis using a weighted probabilistic model of inflammation. They found a reverse J-shaped BMI-death association,

where a higher BMI ($>40 \text{ kg/m}^2$) was associated with a higher death risk, while a lower mortality risk was observed with a BMI $30\text{-}35 \text{ kg/m}^2$ across all CKD stages and for BMI $>40 \text{ kg/m}^2$ in CKD stage 4/5. They concluded that the obesity paradox in this study was consistent in advanced CKD including in their bias analysis, suggesting that inflammation may not fully explain the observed paradoxical BMI-mortality associations.²⁹ Whether functional nutrition can be employed for weight management, without deleteriously affecting survival, remains to be seen in future studies.

Vengalasetti et al³⁰ studied the association of dysgeusia and dysosmia, assessed by the Chemo-Sensory Questionnaire, and CKD in the National Health and Nutrition Examination Survey (NHANES) 2011-14 and found that non-dialysis CKD was significantly associated with dysgeusia and the association with dysosmia was of borderline significance. It is not clear whether functional nutrition can favorably affect the perception of taste and smell and have salutary impact on holistic health including CKD related outcomes.

McFarlane et al³¹ studied the associations between diet quality, uremic toxins, and gastrointestinal microbiota via metagenomic sequencing in a cross-sectional study of 68 adults with CKD, randomized to prebiotic and probiotic supplementation while assessing diet quality using a plant-based diet index including dietary protein-to-fiber ratio. They found that dietary fiber intake was associated with lower levels of indoxyl sulfate, whereas the healthy plant-based diet index was associated with lower levels of free p-cresyl sulfate, and that a higher protein-to-fiber ratio was associated with unfavorable microbiome features.³¹ Hence, diet quality may influence uremic toxin generation and gut microbiota, composition, and functional diversity in persons with CKD, aligned with the potential role of functional nutrition in the management of CKD.

Betz³² conducted a survey among 644 kidney professionals to examine perception of recommendation of plant-based diets for CKD management. The majority of survey participants were dietitians (58%), worked in dialysis clinics (54%), had heard of using plant-based diets for kidney disease (88%), and believed it could improve CKD management (88%). Dietitians were more likely to report plant-based diets as beneficial and felt more confident in their ability to plan a balanced plant-based diet compared with other specialties.³² The identified awareness of the benefits of plant-based diets in kidney disease can set the stage for more effective implementation of functional nutrition including in the era of value-based kidney care models.

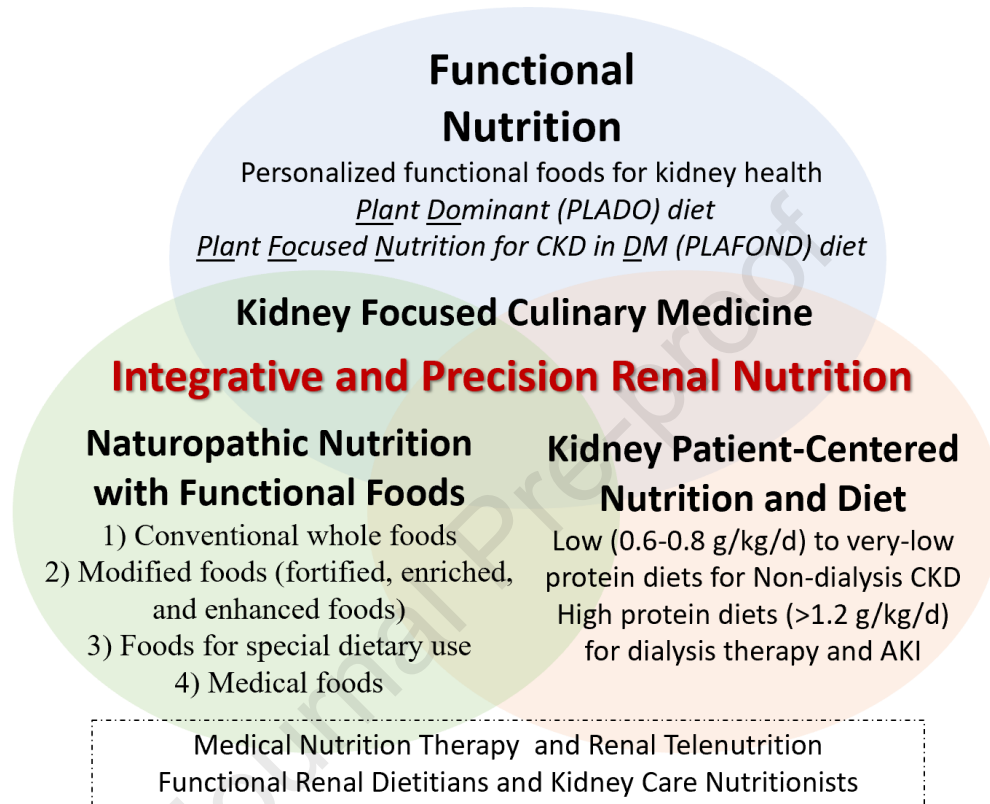
Other articles of this issue of the journal include the study by Lu et al,³³ who examined malnutrition risk and kidney function decline in 786 community-dwelling older adults in Singapore; Sa Martins et al,³⁴ who examined the prognostic value of the Malnutrition-Inflammation Score or Kalantar Score in hospitalization and mortality in 2,444 long-term hemodialysis patients from 25 centers in Portugal with a median period of 45-month follow-up; Lin et al,³⁵ who conducted a case-controlled study in 11 patients with ESRD and 11 healthy volunteers to study the accumulation of gut microbiome-derived Indoxyl Sulfate and P-Cresyl Sulfate in ESRD; Liao et al,³⁶ who reports an association between iron deficiency and platelet count elevation in 1,167 dialysis-dependent patients in China; Chen et al,³⁷ who report their prospective pilot study of the efficacy of roxadustat for erythropoietin hypo-responsiveness in 50 patients on peritoneal dialysis; Yang et al,³⁸ who studied the predictive value of objective nutritional indexes in technique failure in 276 patients on peritoneal dialysis; and Proano et al,³⁹ who presented the design of a prospective study to examine the implementation of evidence-based Kidney Nutrition Practice Guidelines under RDNs' care for patients with CKD Stage 5

treated by dialysis. Some of the aforementioned studies and reports are relevant to the practice of Functional Nutrition including in the era of Value-Based Kidney Care models.

In conclusion, functional nutrition is an important intercept of precision nutrition and culinary medicine in kidney care and is based on use of functional foods to compliment conventional management strategies in the form of multi-modal, integrative, and holistic nutrition and pharmacotherapy.⁶ Functional nutrition can be effectively implemented by trained renal dietitians and other RDNs to manage kidney health and to prevent or correct protein-energy wasting,⁴⁰ while it can be integrated into the World Kidney Recipes^{10, 41} and help enhance education and health literacy in kidney patients and their care-partners.⁴² Applied functional nutrition benefits from effective MNT strategies^{15, 43} including renal telenutrition as an important goal under the value-based kidney care models²⁴ for secondary and tertiary prevention of CKD,⁴⁴ to ensure more choices for patients with kidney disease^{45, 46} and to overcome disparities in renal nutrition service capacity and education.^{41, 42, 47, 48}

Figure 1. Conceptual model of Functional Nutrition in kidney care and renal medicine.

Abbreviations: AKI: acute kidney injury, CKD: chronic kidney disease, g/kg/d: grams of dietary protein per kilogram body weight pe day.



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Journal Pre-proof

Functional Nutrition

Personalized functional foods for kidney health

Plant Dominant (PLADO) diet

Plant Focused Nutrition for CKD in DM (PLAFOND) diet

Kidney Focused Culinary Medicine

Integrative and Precision Renal Nutrition

Naturopathic Nutrition with Functional Foods

- 1) Conventional whole foods
- 2) Modified foods (fortified, enriched, and enhanced foods)
- 3) Foods for special dietary use
- 4) Medical foods

Kidney Patient-Centered Nutrition and Diet

Low (0.6-0.8 g/kg/d) to very-low protein diets for Non-dialysis CKD
High protein diets (>1.2 g/kg/d) for dialysis therapy and AKI

Medical Nutrition Therapy and Renal Telenutrition
Functional Renal Dietitians and Kidney Care Nutritionists